deepest and the most superficial pixel layers were selected as the deep and superficial regions of interest, respectively, and all the pixel layers in-between those were combined into the middle region of interest. To avoid partial volume artefact, only pixels completely inside the cartilage were included. Triple dose (0.3 mM/kg of Gd-DTPA^{2-}, Magnevist, Bayer Healthcare Pharmaceuticals, Germany) the measurements repeated four times (1-4 h) after an intravenous injection.
Estimated gadolinium concentration for all regions of interest was calculated using the following formula:
$[Gd] = (1/T_{1Gd} - 1/T_{1pre})/r_1$,
where T_{1Gd} is the T_1 value at a certain time point after contrast agent injection, T_{1pre} is the T_1 value before Gd-DTPA^{2-} injection, and r_1 is the relaxivity of Gd-DTPA^{2-}, for which the value 4.1 s^{-1} mM^{-1} measured in human plasma at 37°C temperature was used.
Results: The cartilage thickness ranged from 1 to 5 pixels meaning that the thickness of the middle region varied between 0 and 3 pixel layers.
Pre-contrast, a depth-wise variation of T_1 was observed with 50% higher values in the superficial region compared to the deep region.
The Gd-DTPA^{2-} concentration seemed to remain static between two and three hours in the superficial region, but was still increasing in the middle and deep regions. Between three and four hours, the concentration started to decrease in the superficial region, but still kept increasing in the deep region (Figure 2)

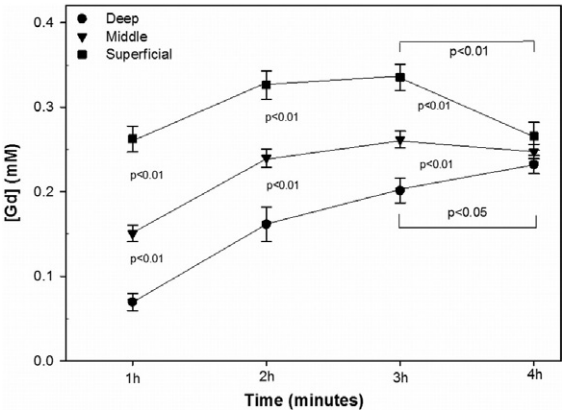

Figure 2

Conclusions: This study clearly demonstrates depth-wise variation in gadolinium concentration at different time points.
The continuous increase in gadolinium concentration up to four hour in the deep region and static state of gadolinium concentration between 2 to 3h followed by decreasing between 3 to 4 h in the superficial region could indicate that most of the contrast comes from the synovial side, whereas the uptake from the bone or subchondral side is negligible. Based on the current results, the ideal time point to observe cartilage seems to be two hours after contrast agent injection, as previously reported, because the bulk change in gadolinium concentration is quite small between two to three hours. However, the ongoing increasing of gadolinium concentration in the deep layer could lead to an overestimation of GAG content in the deep cartilage in vivo. Furthermore, the depth-wise variation of pre-contrast T_1 values suggests that the analysis of bulk cartilage region of interest may not be the optimal way of estimating the GAG content, and that the post-contrast T_1 doesn't provide all needed information for cartilage evaluation.
The present results recommend a depth-wise analysis in clinical dGEMRIC studies, including a deep and superficial region of interest to provide additional information about the status of the cartilage.

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RELIABILITY OF BONE DENSITY MEASUREMENT IN OSTEOARTHRITIS USING DIGITAL RADIOGRAPHIC PROCEDURES

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Purpose: Dual energy X-ray Absorptiometry (DXA) is the method of choice for quantifying bone density (BD). In clinical practice however, BD is commonly subjectively assessed on standard radiographs for the evaluation of (longitudinal) bone changes in osteoarthritis (OA). The transition from conventional radiography to digital radiography needs re-evaluation whether BD can be quantified on radiographs. The objective of this study was to evaluate whether in digital radiographs BD (hydroxylapatite in g/cm^2) can be related to grey value by use of an aluminum step wedge (20 steps from 2 to 40 mm) as a reference for BD (in mm aluminum equivalent=mmAl), independent of radiographic settings.
Methods: A bone density standard (BDS) was created consisting of predefined amounts of hydroxylapatite (eight cups ranging from 0 to 5.75 g/cm^2). BD of the eight hydroxylapatite cups was first measured by use of DXA (Hologic Discovery). Subsequently, digital radiographs of the BDS were acquired (Philips Digital Diagnost), with different settings. Peak voltage (kVp), milliampere seconds (mAs), tube added filtering, and BDS position in the radiographic field were varied. Also the default clinical post-processing module, which is introduced with the development of digital radiography, was compared with post-processing switched off. In all cases a human (cadaver) knee joint was added to simulate clinical conditions, and an aluminum step wedge was added as a potential reference. Custom made software was used to express the grey values in the BDS in mmAl by comparing them to the grey values measured in the step wedge. The grey values in the step wedge were represented by a linear, or a third order polynomial function. Linearity of the relation between actual BD (g/cm^2) and BD in mmAl in the BDS was evaluated.
Results: The relation between actual BD and DXA values of the BDS was strongly linear: R^2=0.99. With a linear representation of the step wedge, the relation between actual BD and BD in mmAl was rather low under regular clinical settings: R^2=0.82. Specifically switching off the post-processing module, improved the linear relation to R^2=0.93. Variation in the other radiographic settings (kVp, mAs, filter, and position) moderately influenced the linearity: R^2=0.72-0.88. When a third order polynomial representation of the step wedge was used, the relation for regular clinical settings improved to R^2=0.96. In this case switching off the post-processing module only slightly improved the relation between actual BD and mmAl to R^2=0.98.
Conclusion: Bone density evaluation on digital radiographs is significantly hampered by the default clinical post-processing module on digital x-ray systems. Also variations in x-ray setting are of influence. However, by use of an aluminum reference wedge and by using a non-linear fit, BD in the range of interest of subchondral bone changes, can be expressed in mmAl rather precisely.
Sponsor: Dutch Arthritis Association (CHECK).
Diclosure Statement: No conflict of interest.
Acknowledgment: We acknowledge the radiology department for their cooperation, and Paco Welsing for statistical support.

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PHOTOGRAPHIC SCORING IS INSENSITIVE FOR MONITORING PROGRESS OF HAND OSTEOARTHRITIS, BUT SIDE BY SIDE COMPARISON OF PHOTOGRAPHS DETECTS PROGRESS AT 5 YEAR INTERVALS IN THE ELDERLY. THE AGES-REYKJAVIK STUDY

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Purpose: In previous studies we have developed a scoring system for diagnosing and estimating the severity of hand osteoarthritis (HOA) in the elderly. In this study we compared HOA scores of photographs taken at five-year intervals.
Methods: 143 (80 females, 63 males, age range 71-91, median age at second photograph 79.5) participants in the Age, Gene/Environment Susceptibility-Reykjavik Study (AGES-Reykjavik) had new hand photographs taken after a five year followup. The photographic procedure was the same as in previous studies with a Fuji Finepix 6800 zoom camera (2800×2200 pixels) on a tripod and a dark velvet board with two small central markers. HOA scoring was twofold, first a blind scoring of 0-3 for DIP, PIP and CMC1 joint groups (1) and secondly a more detailed joint by joint comparison with both photographs side by side. Progress in the IP and CMC1 joints were classified as probable or definite.
Results: There was no significant change in aggregate HOA severity scores

at five years although a slight increase in CMC1 scores was observed. Patterns of involvement were also similar as witnessed by high intra-class coefficients for DIP (0.88), PIP (0.79), CMC (0.73) and aggregate scores (0.87) at five years. On side by side comparison of photographs, 4 subjects (2.8%) had probable worsening and 4 had (2.8%) definite worsening in the IP joints, and in the CMC1 joints 14 (9.8%) had probable and 10 (7.0%) definite worsening. Progress in the CMC1 joints was more apparent in females.

Conclusions: At this age, there is little change in IP joint osteoarthritis and photographic scores do not detect changes after 5 years, although side by side comparison detects occasional worsening. There appears to be more progress of HOA in the CMC1 joints in this age group, but hand position in photographs is very important in estimating OA in these joints and changes in hand posture due to aging and other neuromuscular conditions may exaggerate apparent worsening.

This study confirms the robustness of the photographic method showing high reproducibility at five year intervals. Even in this age group, progress of HOA can be determined on side by side comparison of photographs.

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LOAD RESPONSE OF KNEE CARTILAGE T2 IN PATIENTS WITH MENISCUS DISORDER: EVALUATION USING LOADING IN SITU MRI

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Purpose: The normal meniscus was assumed to distribute the load transmission over the entire surface of the articular cartilage, and meniscus disorder may lead to abnormal load distribution in response to load-bearing, resulting in high prevalence of osteoarthritis progression. Therefore, evaluation of intra-articular biomechanical condition after meniscus injury is important to estimate risk of subsequent progression of osteoarthritis and to decide appropriate treatment methods. Recent studies showed that responsiveness of articular cartilage to compressive loading by T2 value may indicate pressure distribution on the cartilage, via evaluation of dynamic changes in the collagenous architecture or water influx or efflux. We have developed a loading apparatus to apply axial load to the knee joint during MR imaging in order to simulate physiological load-bearing condition while standing. Our objectives were to examine clinical feasibility of cartilage T2 with use of loading in situ MR imaging, for evaluation of abnormal pressure distribution in patients with knee meniscus disorder.

Methods: Thirteen patients with knee injuries (13 knees) and 10 asymptomatic normal volunteers (10 knees) were imaged on a 3.0 T GE MRI scanner using a 8-channel knee phased array coil. The mean age of the patients and volunteers were 34 and 32years, respectively. Among 13 patients, 9 patients had either or both of the medial and lateral meniscus abnormalities and the other 4 patients had ACL or PCL injury without meniscus disorder, which were confirmed by arthroscopy. During MR imaging, the participants was laid on a custom-made loading apparatus, which had a pulley system linked to a sliding foot plate. The shoulders of the participants were strapped tightly, and 50% of the body weight was applied via the foot plate, when loading. On unloading and loading conditions, sagittal T2 maps of the medial and lateral femoro-tibial joints were obtained from multi-echo spin echo sequence with fat-suppression (TR, 1500 ms; 8 echoes between 10.0 ms and 80.0 ms; field of view, 12 cm; matrix, 384×256). On each of medial and lateral mid-sagittal image, the cartilages at the weight-bearing ranging anterior and posterior margins of the meniscus were divided into 3 sections with equal length, and each section was further divided into deep and superficial layers with equal thickness, using a custom-made software (Fig. 1). Change of T2 values by loading in each ROI was compared between patients and normal volunteers, and between joint compartments with and without meniscus tear among patients, using the nonparametric Mann-Whitney U test.

Results: On unloading condition, there was no significant difference of T2 at each ROI between patients and volunteers, except AD of the medial femoral cartilage in which T2 of the patients was significantly higher ($p=0.01$). By loading, T2 was likely to decease at each zone, however, there was no significant difference of T2 change at each ROI between patients and volunteers. Among 13 patients, meniscus tear was noted in 5 knees at the medial side and in 7 knees at the lateral side. In the medial side, T2 at AS of the femoral and tibial cartilages decreased significantly larger in knees without meniscus tear than knees with meniscus tear (Femoral cartilage: -13.3% vs -0.3%, $p<0.05$; Tibial cartilage: -8.2% vs +4.7%, $p<0.05$)

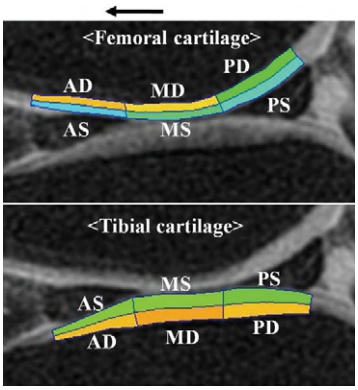

Figure 1. Definition of ROIs at the femoral and tibial cartilage.

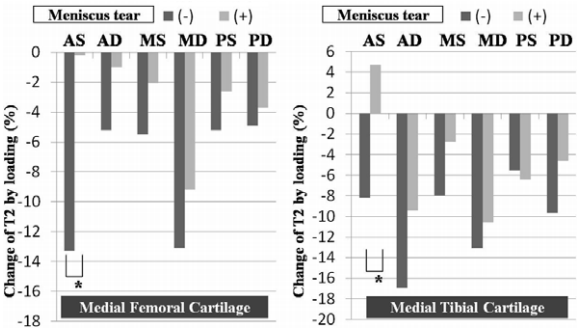

Figure 2. T2 change by loading in knees with and without meniscus disorder (*$p<0.05$).

(Fig 2). In the lateral side, there was no significant difference of T2 decease between knees with and without meniscus tear.

Conclusions: Significantly smaller decrease of T2 in knees with meniscus tear may reflect location-specific load transmission failure associated with the meniscus tear. In this context, T2 evaluation under loading conditions can be expected to provide biomechanical assessment of pathological conditions with respect to localized stress concentration in the cartilage of patients with knee injuries.

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THE NATURAL HISTORY OF OA ASSOCIATED BMLS IN THE OAI PROGRESSOR COHORT

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Purpose: The natural history of osteoarthritis (OA) related bone marrow lesions (BML) is poorly understood. Although it is clear that BMLs are not static, studies have reported conflicting results concerning their turnover and location. Semi-quantitative evaluation has been unable to study the spatial and temporal distribution of BMLs. This study employed a novel statistical model to precisely locate the BMLs within the subchondral bone and generate detailed anatomically relevant maps to track their change in size over time.

Methods: A cohort of 88 subjects was generated from the Osteoarthritis Initiative (OAI) progression groups 0.B.1 (baseline) and 1.B.1 (12-month follow up visit). Subjects had K-L scores of 2 or 3; medial JSN > lateral JSN, medial osteophytes and ≥1° of varus mal-alignment. OA related BMLs were defined as ill-delineated regions of hyperintensity in the subchondral bone, excluding the region adjacent to ligament attachment sites on Turbo Spin Echo magnetic resonance images (MRIs). The slice-by-slice, subvoxel delineation of the lesions across the paired images was blinded to time-point but not to subject using EndPoint software (Imorphics, Manchester, UK). Study reproducibility was determined using a Bland Altman test and the measurement error defined as the smallest detectable difference (95% level of agreement). BML depth with respect to the adjacent bone surface was calculated using an adapted method previously utilised for articular cartilage thickness measurement. A statistical bone model was